Remarks

This is in response to the April 8, 2011 Office Action in the above-referenced patent application. This Reply is being submitted within three months of the mailing date of the Office Action. No petition or fee for extension of time is believed to be required.

Status of the Claims

Claims 1-2, 5-6, 8-22, 24, and 27-43 were pending for purposes of the current Office Action, although claims 6, 11-14, 24, and 27-42 have been withdrawn from consideration. Claims 2 and 10 have been canceled in this amendment. Claims 3-4, 7, 23, and 25-26 were previously canceled. Accordingly, claims 1, 5, 8-9, 15-22, and 43, as amended, remain pending and under consideration.

Claim 1 has been objected to, and all pending claims are currently rejected.

Claim 1 Objection

Claim 1 is objected to for the recitation of both "inactive segment" and "inactive composition" which are considered in the Office Action to refer to the same thing. To clarify, the "inactive composition" is the "fill" material, e.g., a granulation or powder, used in the formation of the "inactive segment" by the compression step. Thus, the "inactive composition" is different in time from the "inactive segment." Nevertheless, applicants have amended claim 1 to delete any reference to "immediate release composition" or "immediate release segment."

Reconsideration and withdrawal of this objection is respectfully requested.

Double Patenting Rejections

The claims remain rejected on the ground of non-statutory obviousness-type double patenting over claims 1-20 of US 7,329,418. A new Terminal Disclaimer will be submitted to obviate this double patenting rejection upon an indication of allowability of claims in the subject application.

Claims 1-2, 5 and 16 are newly rejected on the ground of non-statutory obviousness-type double patenting over certain claims of US 7,622,137. A Terminal Disclaimer will be submitted to obviate this double patenting rejection upon an indication of allowability of claims in the subject application.

The acceptance and recording of the Terminal Disclaimers regarding US Application Ser. Nos. 10/598,267 and 11/569,343 are gratefully acknowledged.

New Rejection Under 25 USC §112

Claim 1 has been rejected under 35 USC §112, first paragraph as lacking written description for the recitation of "immediate release inactive composition" and for the recitation of "two layers and three or more segments." Applicants respectfully request reconsideration in view of the amendments to the claims which have removed the objected-to language. Because the objections are now moot, applicants respectfully request withdrawal of the rejection.

Claim 1 is further rejected under 35 USC §112, second paragraph, as being unclear regarding the recitation of "an immediate release inactive composition." As stated above, a person of ordinary skill in the pharmaceutical tableting arts would readily understand and recognize the term "excipient known for use in immediate release pharmaceutical formulations" to refer to an excipient that provides "immediate release" characteristics to a dosage form when an active drug is present.

The term, "excipient known for use in immediate release pharmaceutical formulations" is supported in the subject application in the DESCRIPTION OF MANUFACTURE OF PREFERRED EMBODIMENTS section at pages 27-28, wherein the middle "inactive" segment is manufactured using Nu-Tab® (Compressible sugar 30/35 N.F.) or, alternatively, a mixture of:

Dibasic calcium phosphate anhydrous,
magnesium stearate, and
PVP K-30.

These excipients are well known in the art for use in immediate release pharmaceutical formulations in view of their known properties of readily dissolving when administered or ingested. Accordingly, an "excipient known for use in an immediate release pharmaceutical formulation" would be clear and definite in its meaning to a person of ordinary skill in the art.

Reconsideration and withdrawal of the rejections under 35 USC §112, first and second paragraphs, is respectfully requested.

New Rejection under 35 USC §103

The pending claims are newly rejected under 35 USC 103(a) as being unpatentable over US Pat. Appl. Pub. No. 2004/0234608 (the "'608 application") in view of US 4,215,104 (the '104 patent) and PCT Publication No. WO 00/18447 (the "WO'447 application").

Applicants respectfully traverse. This newly asserted obviousness rejection is based on the untenable conclusion that the cited references, taken together, teach or suggest the claimed layered (segmented) tablets having an inactive segment, which consists of excipients that are known for use in pharmaceutical formulations (referred to hereinafter as "IR excipients"), between two active segments. A close review of the cited references shows that the cited references do not teach or otherwise suggest layered (segmented) tablets that are taller than wide, and having inactive portions consisting of IR excipients disposed between two active segments.

Distinguishing these references separately and individually, the primary cited reference, the '608 application, concerns tablets which are NOT immediate release tablets and do not include inactive layers consisting of IR excipients. The '608 application describes a Gastric Retention Delivery System (GRDS) – a dosage form which *controls the release* of the active drug by retaining the dosage form in the stomach, i.e., a "controlled release" dosage form – using an inactive portion, or "shell," comprising a "swellable" hydrogel which in all cases has controlled release properties.

The hydrogel used in the dosage forms described in the '608 application is a hygroscopic material which absorbs water or aqueous liquid such as gastric fluid, causing the hydrogel to swell. This swelling property results in a physical increase in size of the dosage form to prevent the dosage form from passing through or emptying from the stomach for a prolonged period of time. The hydrogel also creates a thick barrier through which the release of drug (even from an IR core or reservoir) is slowed.

The Office Action correctly points out that the '608 application includes embodiments wherein the active portion in the reservoir of the dosage form is in "immediate release" form; however, those embodiments still relate to, and require, a final dosage form having the described Gastric Retention Delivery System (GRDS) of the invention, which includes the controlled release inactive portion or hydrogel shell. Thus, the dosage form described in the '608 application is a controlled release dosage form, since the '608 application expressly states, in paragraph [0034] that the inactive portion (the shell) swells so that the dosage form is "retained in the stomach for a prolonged period of time."

According to the definition provided in the '608 application, "controlled release" is defined as "any release other than immediate release," (see paragraph [0033], page 4, col. 2). Such action for a "prolonged period of time" cannot be a composition containing only immediate release excipients, and a tablet of the '608 application cannot be an "immediate release pharmaceutical tablet" as expressly claimed for the subject invention.

The claimed invention is further distinguished and unobvious from the dosage forms described in the '608 application in that the claimed invention comprises an inactive segment that is adapted to be broken for dividing the dose prior to administration. The swellable inactive portion of the dosage form described in the '608 application (which, again, is not an immediate release formulation), is provided to facilitate gastric retention of the dosage form and allow delivery of the active ingredient while the dosage form is retained in the stomach.

The inactive swellable portion of the dosage form described in the '608 application must remain intact prior to its administration in order to provide its intended utility of gastric retention. The inactive swellable portion described in the '608 application is therefore not adapted to be broken or divided prior to administration of the tablet, and cannot serve its intended purpose if broken or divided. If broken or divided, the dosage form of the '608 application would lose its gastric retentive function, becoming inoperable for that intended purpose. Clearly, the primary reference does not provide a teaching or suggestion of the claimed invention, and cannot be modified to provide a tablet of the subject invention without destroying its operability.

Neither do the secondary references (the '104 patent or the WO'447 application) cure the defects of the '608 application. The '104 patent does not relate to layered or segmented tablets, as claimed. According to the Office Action, the '104 patent is cited for its description of multi-fractionable tablets having separation marks for divisibility of the tablets. However, because the dosage forms of the '608 application cannot be divided without destroying their intended purpose and operability, the '104 application cannot be properly combined with the '608 application to arrive at the subject invention.

The Office Action further alleges that the '104 patent describes taller-than-wide tablets. However, the '104 patent relates only to homogenous compositions forming a tablet formed as a single layer. At page 9 of the subject application, the tablets are expressly described as being "non-homogeneous." There is no teaching or suggestion in the '104 patent of an inactive portion of the tablet provided as a middle layer – especially an inactive portion that forms a discrete middle segment adapted to be broken for dose division (without breaking through an active-containing portion of the tablet) as described and claimed for the subject invention. Accordingly, the '104 patent fails to cure the defect of the primary reference, the '608 application.

In addition, it is respectfully noted that the tablets of the '104 patent are compressed in the tablet die in a wider-than-tall configuration, not a taller-than-wide configuration as claimed for the subject invention. This is clear from the formation of the scores shown for the tablets of the '104 patent. The embossing forming the scores or separations in the

tablets of the '104 patent must be on the top or bottom punch used in the tablet press. An embossing on the side of the tablet die would impede and not allow extraction of the tablet from the die following compression. Therefore, applicants maintain that the tablets of the '104 patent are not "taller-than-wide."

The other secondary reference (the WO'447 application) cited in the obviousness rejection concerns an inactive portion (enveloping active tableted cores) which is always provided as an extended release formulation. Administration of the tablet as described in the WO'447 application would provide controlled release of the actives – even from tablet cores that are formulated as immediate release compositions – because the active compositions are enveloped by and contained within the extended release inactive portion. Accordingly, the tablet described in the WO'447 application is also a controlled release tablet.

Applicants respectfully submit that the WO'447 application does not describe or even suggest an immediate release tablet as claimed for the subject invention, nor does the WO'447 application describe or suggest a tablet having an inactive segment consisting of IR excipients.

The WO'447 application describes immediate release formulations only for the *active* portions. The inactive portion of the tablet described in the WO'447 application is always a controlled release formulation (see, e.g., p.1, lines 8-10 reciting "two immediate release compartments substantially enveloped by a [an inactive] scored extended-release compartment." The WO'447 application therefore fails to cure the defect of the '608 application relating to its failure of teaching or suggesting an immediate release divisible tablet.

Further, the '447 application does not cure the defect of the '608 application regarding its failure to teach or suggest a tablet in a taller-than-wide configuration. The tablet cores in the controlled release envelope of the '447 application cannot be formed as taller-than-wide tablets in their final dosage form because the cores are first compressed in a conventional single layer tablet press, then "press-coated" to form the final dosage form.

It is well known that a conventional press coating process forms a tablet in a wider-than-tall configuration.

Moreover, those core tablets must be oriented next to one another – side-by-side, horizontally, and cannot be oriented one on top of the other (vertically) to achieve a press coated final dosage form. There is no teaching or suggestion provided in the '447 application or anywhere in the cited references to modify the conventional tableting of the cores, or the press-coating process to produce a tablet that is taller-than-wide, in the tablet die, as claimed for the subject invention.

In summary, the '104 application cannot be properly combined with the '608 application and, even when combined, the '608 application, the '104 application, and the WO'447 fail to teach or suggest the subject invention as claimed. In view of the defects of the teaching of the '608 application, and the failure of the secondary references to cure those defects, applicants maintain that the claimed invention would have been unobvious in view of the cited references, whether taken alone or in combination. Accordingly, withdrawal for the rejection under 35 USC §103(a) is respectfully requested upon reconsideration of the claims as currently amended.

The claims are further rejected under 35 USC 103(a) as being unpatentable over US Pat. Appl. Pub. No. 2004/0234608 (the "'608 application") in view of US 4,215,104 (the '104 patent) and PCT Publication No. WO 00/18447 (the "WO'447 application") and further in view of US Patent Nos. 5,118,021 (the "'021 patent") and 4,509,589 (the "'589 patent").

Applicants incorporate by reference and reiterate that the '608 application, the '104 patent, and the WO'447 application failed to make obvious the claimed invention. The '021 patent and the '589 patent, which are apparently cited for their description of separation marks, including printed indicia, in the tablets add nothing to cure the defects or deficiencies present in the teaching of the other cited references.

Because these cited references, separately and combined, fail to teach or suggest the claimed invention, applicants respectfully submit that the claimed invention would not have been obvious in view thereof. Reconsideration and withdrawal of the rejection under

35 USC 103(a) citing the '608 application in view of the 104 patent or the WO'447 application, and further in view of the '021 and the '589 patents, is respectfully requested.

The claims are also rejected under 35 USC 103(a) as being obvious over PCT Publication No. WO 00/18447 (the "WO'447 application"), in view of EP 0348683 (the "EP'683 application") and Pharmaceutical Industry Info 2002 (PII2002) and further in view of US Patent Nos. 5,118,021 (the "'021 patent") and 4,509,589 (the "'589 patent").

The Office Action relies on the following point in support of this rejection:

- The '447 describes two immediate release drug dose packages with identical drug(s) that are greater in height than the inactive component.

In addition to the admission in the Office Action that the WO'447 application does not teach an IR inactive component, it is respectfully pointed out that the WO'447 also fails to teach or suggest that the tablet (the final dosage form) is formed in a taller-than-wide configuration. A tablet characterized as in the above point still fails to meet the claim requirement of a dosage form, itself, having a height greater than its width as measured *in the tablet die* during or following compression.

As explained above, the WO'447 application cannot be formed in a "taller-than-wide" configuration due to the limitations of the press coating process. The EP'683 application does not cure the defects of the WO'447 application. EP'683 describes a three layer tablet having an inactive layer for separating incompatible actives in the other two layers. The EP'683 application fails to describe a tablet that is taller-than-wide and having a middle inactive layer that is greater in height than the combined height of the active layers, as claimed. Specifically, the EP'683 application describes an inactive middle layer that is no more than 40% of the height of the tablet. By definition, a tablet of the subject invention has a middle layer greater than 50% of the total tablet height.

This distinction has importance in the way the tablets are used. Tablets described in the EP'683 application have a middle layer provided solely to separate incompatible actives. In tablets of the subject invention, the middle inactive layer is adapted to be broken for dividing the dose prior to administration. The concept of dose division by breaking the

middle layer is not taught or suggested by the EP'683 application. The inclusion of the inactive middle layer in tablets of the EP'683 application is to provide a combination product where the two actives can be administered together, and not divided prior to administration.

The Office Action cites the 2002 Pharmaceutical Industry Info. reference (2002 PII), disclosing the Korsch TRP 700/900, for its teaching of the capability to make a taller-than-wide tablet. However, applicants respectfully submit that the 2002 PII reference does not cure the defects of the WO'447 application nor the EP '683 application. Indeed, even when combined, the EP '683 and 2002 PII references still fail to teach or suggest an IR layered tablet having a middle inactive segment which advantageously serves as a discrete breaking layer or segment.

The 2002 PII reference discloses the Korsch multilayer tablet press – a device and process accepted in the art as useful for manufacturing controlled-release (CR) tablets. Specifically, the Korsch tablet press provided for the manufacture of a tablet having an expandable "push layer" which enabled the release of a drug to be modified. These push layers expand when contacted by aqueous solution to force solubilized active ingredients (in a separate layer) through an opening in the tablet coating. These coatings are typically insoluble in the aqueous solution in order to provide a relatively rigid surface against which to "push" and provide the force for excreting the drug composition. Moreover, these inactive push layers were provided at one end of the tablet, not between two active layers, and were not intended to be broken through in order to divide the dose or doses provided in the whole tablet as claimed for the subject invention. Applicants believe there is no reasonable nexus between the IR layered tablets of EP '683 and the manufacturing device and process for manufacturing CR tablets containing a "push layer" as described in the 2002 PII reference.

The inactive push layer in tablets manufactured in accordance with the PII 2002 reference was not intended to be broken through in order to divide the dose or doses in the whole tablet, as claimed for the subject tablet, because of the rigid coating required on a tablet made by the process contemplated by the PII 2002 reference. Conventional breaking techniques, such as breaking by hand, make it difficult if not practically impossible to break through the tablets made in accordance with the known process using the Korsch multilayer tablet press. Also, breaking through an inactive push layer of the prior art "controlled-release" tablets can render such tablets inoperable. Accordingly, applying or combining the knowledge of

using a Korsch multilayer tablet press with the layered immediate release tablets of EP '683 goes completely against the teaching of the subject invention

Thus, other than the impermissible use of applicants' own disclosure as a basis for hindsight reconstruction of the claimed invention, the motivation to combine these two cited references and their combined teaching or suggestion of the claimed invention appear to be absent. Applicants respectfully maintain that nowhere in EP '683 or the 2002 PII references is there any disclosure directing or motivating a person of ordinary skill in the art toward the specific active/inactive/active taller-than-wide configuration in a three-layer, immediate-release tablet as expressly claimed. And nowhere in EP '683 or the 2002 PII reference is there any disclosure directing or motivating a person of ordinary skill in the art toward a tablet which provides the specific advantages achieved by the claimed tablet configuration.

The claimed invention as a whole, and as currently claimed, provides unique properties which were unavailable from the tablets described in the cited references. These unique properties of the claimed invention further provide unique advantages that were unforeseen by persons of ordinary skill in the art having access to, or knowledge of, the cited references.

The "taller-than-wide" configuration of the claimed tablets (as it sits in the compression die) lends itself to having the vertical axis as its long axis. By having an inactive segment between two active segments in a taller-than-wide tablet, as claimed, the inactive segment can advantageously be useful as a breaking segment. This provides that the area around the midline of the vertical axis is the most advantageous area for breaking the tablets in half – and through the inactive middle segment – such that no breakage occurs to the active end segments.

Because breakage will occur easiest "across" the short (horizontal) axis of the tablet, the claimed taller-than-wide tablet can break through a single layer, i.e., the inactive segment. Breakage in this manner allows physical separation of the active "end" segments from one another without breaking through any part of those active segments. Therefore, the active segments can remain intact even after the whole tablet is divided into two or more portions. This feature can advantageously prevent any loss of active during the breaking of the tablet. The standard wider-than-tall tablet, as known in the art, cannot provide this advantage, even if it includes an inactive segment between two active segments because the short axis is oriented "across" the layers.

Advantageously, the claimed invention, having an inactive middle segment as its breaking segment, allows the tablet to be broken so that the break is confined to that inactive segment. In such case, there is no breakage through any portion containing active substance, thus preventing loss of active ingredient from any resulting tablet portion, even when the broken edges (of the inactive segment) may chip or crumble.

The innovation arrived at for the subject taller-than-wide tablets originated from the unique motivation to provide a tablet readily breakable into precise partial doses and thereby allowing flexible dose adjustment and titration under a single prescription and a single visit to the physician. Applicants have therefore developed an entirely new compressed tablet configuration which addresses an unmet need.

The secondary'021 and '589 patents are then cited for their description of separation marks, including printed indicia, in the tablets. However, neither of these secondary references cure the defects of the EP'683 or WO'447 applications, or the 2002 PII reference. Because these cited references, separately and combined, fail to teach or suggest the claimed invention, applicants respectfully submit that the claimed invention would not have been obvious in view thereof. Reconsideration and withdrawal of the rejection under 35 USC 103(a) citing the WO'447 application in view of the EP'683 application, and 2002 PII, and further in view of the '021 and the '589 patents is respectfully requested.

Applicants believe that the pending claims, as amended, are in condition for allowance and respectfully request issuance of a Notice of Allowance.

Applicants invite the Examiner to contact the undersigned at the address and/or phone number provided below if clarification or additional information is needed on any of these matters.

Respectfully submitted,

Dated: July 8, 2011

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